PATENT APPLICATION

Database of Body Surface ECG P Wave Integral Maps for Localization of Left-sided Atrial Arrhythmias

INVENTORS

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CROSS-REFERENCE TO RELATED APPLICATIONS

This application is cross-referenced to and claims priority from U.S. application 09/809,719 filed 03/14/01, U.S. application 09/808,728 filed 03/14/01, provisional U.S. application 60/196,204 filed 04/11/00, and U.S. application 09/724,947 filed 11/28/00, all of which are incorporated herein by reference.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

FIELD OF THE INVENTION

This invention relates generally to a method for classification and localization of arrhythmias. More particularly, the present invention relates to a system for developing a database of body surface electrocardiogram (ECG) P wave data maps for localization of the origin of left-sided atrial arrhythmias.

BACKGROUND ART

Early investigations utilizing atrial pacing in man to study the variations in scalar ECG morphology and vector loop of the P wave with varying sites of focal atrial origin, were primarily geared towards the differentiation of left- from right-sided atrial rhythms (*e.g. Massumi R.A. and Tawakkol A.A. (1967), Direct study of left atrial P waves, Am. J. Cardiol. 20:331-340; and Harris B.C. et al. (1968) Left atrial rhythm; Experimental production in man, Circulation 37:1000-1014*). Despite several attempts to develop a set of morphologic ECG criteria specific to a left-sided origin of an ectopic atrial rhythm, different algorithms were proposed and consensus appeared difficult to attain.

Mirowski in 1967 initially suggested that a negative P wave polarity in lead I and a "dart and dome" configuration in V_1 was related to a left-sided origin and later added that a negative P wave in V_6 was more specific particularly when the aforementioned features were absent (*Mirowski M. (1967) Ectopic rhythms originating anteriorly in the left atrium; Analysis of 12 cases with P wave inversion in all precordial leads, Am. Heart J. 74:299-308*). Although these findings were partly underlined by others (*e.g. Leon D.F. et al. (1970) Right atrial ectopic rhythms; Experimental production in man, Am. J. Cardiol. 25:6-10*), Harris et al. in 1968 (same reference as mentioned above) contested the importance of P wave inversion in

leads I and V_6 for a left-sided rhythm and alternatively proposed that a terminally positive P wave in V_1 was a more specific finding for a left atrial origin. Conversely, Massumi and Tawakkol (same reference as mentioned above) noted a profound variability in P wave morphology after electrically stimulating the left atrium from similar anatomical sites in different patients and did not believe that distinct ECG criteria specific to areas of ectopic left atrial impulse formation could be developed.

Using temporarily implanted pacing wires following cardiac surgery, Maclean et al. subsequently performed a comprehensive study in 69 patients by stimulating both atria at a total of 12 epicardial regions (*Maclean W.A.H. et al. (1975) P waves during ectopic atrial rhythms in man; A study utilizing atrial pacing with fixed electrodes, Circulation 52:426-434*). Overall the results of this study were disappointing in that only a few specific correlations between P wave morphology and site of origin could be made: (1) a negative P wave in the inferior leads with pacing of the inferior regions in either atrium; (2) a negative P wave in lead I with left atrial pacing near the left pulmonary veins; (3) a positive bifid P wave in V_1 with pacing near the lower pulmonary veins and coronary sinus. Therefore, these investigators and recently others using contemporary multisite endocardial catheter mapping techniques (*Man K.C. et al. (1996) Spatial resolution of atrial pace mapping as determined by uniploar atrial pacing at adjacent sites, Circulation 94:1357-1363*), underline the complexity of visual analysis of the low-voltage P wave and concluded that the 12-lead ECG was of limited clinical value in localizing ectopic atrial foci.

The limited role of the standard 12-lead ECG to distinguish right from left atrial focal activity has also been reported by Kalman et al. during ablation of atrial tachycardia guided by intracardiac echocardiography (*Kalman J.M. et al. (1998) "Cristal tachycardias": origin of right atrial tachycardias from the crista terminalis identified by intracardiac*

echocardiography, J. Am. Coll. Cardiol. 31:451-459). Kalman et al. reported that the P wave morphology on the 12-lead ECG of tachycardias arising from the upper part of the crista terminalis in the right atrium or the right upper pulmonary vein in the left atrium, demonstrates considerable overlap due to the proximity of both structures. Tang et al. suggested previously that a change in P wave morphology in lead V_1 from biphasic during sinus rhythm to completely positive during tachycardia would be helpful in discriminating foci arising from the superior portion of the crista terminalis and the right upper pulmonary vein *(Tang C.W. et al. (1995), Use of P wave configuration during atrial tachycardia to predict site of origin, J. Am. Coll. Cardiol. 26:1315-1324)*. The latter finding was found to be predictive for right upper pulmonary vein tachycardia foci even when lead aVL would demonstrate a positive instead of a negative P wave.

There have also been attempts to localize the atrial insertion site of an accessory pathway during orthodromic atrioventricular (AV) reentrant tachycardia. Farshidi et al. initially demonstrated that a negative retrograde P wave in lead I was associated with a left-sided atrial insertion of the accessory pathway *(Farshidi A. et al. (1978) Electrophysiologic characteristics of concealed bypass tracts: clinical and electrocardiographic correlates, Am. J. Cardiol. 41:1052-1060)*. Garcia Rivera et al. was able to separate free wall accessory pathway locations in the left and right atrium using the retrograde P wave polarity in leads I and V_1 *(Garcia Rivera R. et al. (1980) Retrograde P wave polarity in reciprocating tachycardia utilizing lateral bypass tracts, Eur. Heart J. 1:137-145)*. Other investigators have later studied the localization resolution of the 12-lead ECG for this particular application by confining pace mapping to the annular regions of the left and right atrium (e.g. *Fitzgerald D.M. et al. (1996) P wave morphology during atrial pacing along the atrioventricular ring; ECG localization of the site of origin of retrograde atrial activation, J. Electrocardiol. 29:1-10)*. However, despite a more directed pace mapping approach, the paced P wave

morphology only allowed a gross separation of pacing sites in terms of a left- versus right-sided origin, an inferior origin in either atrium, or an origin in the right free wall. In contrast, Tai et al. recently reported that the polarity of the retrograde P wave in leads I, II, III, aVF, and V_1 obtained during AV reentrant tachycardia allows accessory pathway localization to 9 possible annular regions with an overall accuracy of 88% provided a clearly visible P wave could be discriminated (*Tai C.T. et al. (1997) A new electrocardiographic algorithm using retrograde P waves for differentiating atrioventricular node reentrant tachycardia from atrioventricular reciprocating tachycardia mediated by concealed accessory pathway, J. Am. Coll. Cardiol. 29:394-402*). It has also been realized with this application of the surface ECG, that visual analysis of the low-voltage retrograde P wave is frequently hampered by the simultaneous occurrence of the preceding cardiac cycle's high-voltage TU wave.

As mentioned above, visual inspection of the 12-lead ECG in an attempt to correlate changes in P wave morphology and polarity with various locations of ectopic activity is hampered by a low-amplitude signal which is often buried in the preceding TU wave, and also by inter-patient inconsistency in P wave pattern with comparable locations of ectopic left atrial activation, and poor overall spatial resolution in both the left and right atrium. It has been recently demonstrated using right atrial pace mapping that a significantly higher electrocardiographic localization resolution is clinically feasible when multi-lead ECG techniques are adopted (*SippensGroenewegen A. et al. (1998) Body surface mapping during pacing at multiple sites in the human atrium; P wave morphology of ectopic right atrial activation, Circulation 97:369-380*).

There is one preliminary clinical report investigating the use of multi-lead ECG or body surface mapping to discriminate ectopic left atrial activation (*Kawano S. and Hiraoka M.P. (1995) P wave mapping in ectopic atrial rhythm. In: Yasui S. et al. Eds. "Advances in Body*

Surface Mapping and High Resolution ECG": Nagoya, Japan: Life Medicom pp. 47-56).
Kawano and Hiraoka showed that endocardial pacing at one right (low) and three left (low, middle, and high) atrial locations produced characteristic P wave body surface potential map patterns. Access to the latter left atrial locations was attained exclusively through the coronary sinus. However, only a moderate number of pacing site locations were studied while pacing from the pulmonary veins was not attempted.

It is clear that the development of noninvasive methods for clinical localization of left atrial arrhythmias with sufficient and high electrocardiographic resolution is difficult. Therefore, noninvasive localization of left atrial arrhythmias is in need of alternative methods that enable improved discrimination and differentiation of electrocardiographic P wave patterns or morphologies.

OBJECTIVES AND ADVANTAGES

In light of the above, it is the primary objective of the present invention to provide a system for developing a database of body surface ECG P wave data maps. Body surface ECG mapping can be applied to improve noninvasive localization of left atrial arrhythmias prior to radiofrequency catheter ablation.

It is an additional object of the invention to provide a method of storing a database of mean body surface ECG P wave data maps in a computer-readable medium for retrieval, analysis and sharing.

It is an additional object of the invention to provide a database that will enable detailed noninvasive localization of left atrial arrhythmias so that invasive catheter mapping may be targeted and minimized to a small confined segment of the left atrium prior to ablation therapy delivery.

The advantage of the present invention is that the present invention results in shorter and more efficient mapping and ablation procedures with less fluoroscopic exposure of the patient and physician. Additionally, the patient will undergo less trauma and benefit from reduction 5 in the risk for clot formation and stroke since the time required for catheter manipulation in the left atrium can be significantly reduced.

An additional advantage is that the database can be used in an outpatient clinic or physician's office to noninvasively screen patients and map the arrhythmia's origin before admitting a 10 patient to the electrophysiology laboratory to undergo ablation therapy. This noninvasive diagnosis and screening will also enable improved decision making regarding the optimal choice of therapy, e.g. anti-arrhythmic drugs, permanent pacing, ablation treatment, or combinations of these treatment modalities. Another advantage of the present invention is that it will also allow for noninvasive follow-up of patients with left atrial arrhythmias after 15 therapy delivery to assess arrhythmia recurrences due to treatment failure or disease progression.

SUMMARY

20 The present invention provides a method for classification and localization of arrhythmias. More specifically, the present invention provides for a system for developing a database of body surface ECG P wave data maps for classification and localization of left-sided atrial arrhythmias.

25 In accordance with exemplary embodiments of the present invention the method generally comprises receiving P wave data from two or more subjects; computing maps of the P wave

data; classifying the maps and thereby creating classified maps; verifying the classified maps; averaging the classified and verified maps and thereby creating mean maps; and storing and accessing the mean maps in the database.

5   The P wave data may generally be obtained in a subject by electrically stimulating or pacing the left atrium using a probe by for example a retrograde aortic or a transseptal procedure. Alternatively, the P wave data may also be obtained during a spontaneously occurring or induced left atrial arrhythmia.

10   The maps may be computed from the P wave data in the form of P wave potential maps or P wave integral maps. The maps are classified based on spatial pattern characteristics.

The maps may be verified before averaging. The mean maps may then be calculated from the verified maps to construct a database of characteristic body surface ECG mean P wave maps

15   specific to the origin of left atrial pacing or left atrial arrhythmia. The mean maps of the P wave data in the database can be used to automatically classify and localize P wave data from a patient obtained from a left atrial arrhythmia. For instance, P wave data can be obtained from an atrial tachycardia whereby the origin is localized, a focal atrial fibrillation whereby the origin of a single atrial premature beat or an initiating beat is localized, or an orthodromic

20   AV reentrant tachycardia involving an accessory pathway whereby the atrial insertion of an accessory pathway is localized.

BRIEF DESCRIPTION OF THE FIGURES

25   The objectives and advantages of the present invention will be understood by reading the following detailed description in conjunction with the drawings, in which:

8

FIG. 1 depicts an overview of the development of a database of mean body surface ECG P wave data maps for classification and localization of left atrial arrhythmias according to an embodiment of the present invention.

FIG. 2 depicts a system for developing a database of mean body surface ECG P wave data maps for classification and localization of left atrial arrhythmias to better classify and localize left atrial arrhythmias in patients according to an embodiment of the present invention.

FIG. 3 depicts a method for separating obscured P waves from a superimposed QRST complex according to an embodiment of the present invention.

FIG. 4 depicts a method for selecting and processing good quality signals according to an embodiment of the present invention.

FIG. 5A depicts a sensor system having an array of sensing locations distributed across a subject's torso surface according to an embodiment of the present invention.

FIG. 5B depicts a body surface P wave integral map; a plot of a data matrix generated by mapping the integral values with positions corresponding to the location of the sensors across a subject's torso surface according to an embodiment of the present invention.

Fig. 5C depicts an ECG tracing illustrating a method for calculating an integral value across a selected time interval of a heart signal cycle from a single sensor location according to an embodiment of the present invention.

Fig. 6 depicts six mean body surface P wave integral maps obtained during pacing at the left upper or left lower pulmonary vein according to an embodiment of the present invention.

FIG. 7 depicts a database of 17 different mean P wave integral maps generated by left atrial pacing according to an embodiment of the present invention.

FIG. 7A depicts different mean P wave integral maps and their associated segments of pacing origin represented in a postero-anterior view of the left atrium according to an embodiment of the present invention.

FIG. 7B depicts different mean P wave integral maps and their associated segments of pacing origin represented in an antero-posterior view of the left atrium according to an embodiment of the present invention.

FIG. 7C depicts different mean P wave integral maps and their associated segments of pacing origin represented in a left posterior oblique view of the left atrium according to an embodiment of the present invention.

FIG. 8 depicts the design of an apparatus for classifying and localizing left-sided atrial arrhythmias according to an embodiment of the present invention.

FIG. 9 depicts a block diagram of storing a database of mean body surface ECG P wave data maps in a computer-readable medium for retrieval, analysis and sharing according to an embodiment of the present invention.

DETAILED DESCRIPTION

Although the following detailed description contains many specifics for the purposes of illustration, anyone of ordinary skill in the art will readily appreciate that many variations and alterations to the following exemplary details are within the scope of the invention. Accordingly, the following preferred embodiment of the invention is set forth without any loss of generality to, and without imposing limitations upon, the claimed invention.

The present invention involves a system for developing a database of body surface ECG P wave data maps which allows a more intuitive and direct interpretation of the heart signals in terms of the underlying cardiac source. This database enables detailed noninvasive

localization of left atrial arrhythmias by correlating subtle spatial differences in P wave morphology with various locations of ectopic atrial activity. The database is derived from P wave data of two or more subjects but can after its development be updated using additional and/or future P wave data of subjects to improve its resolution for discriminating focal atrial

5   activity.

Clinical application of the database of P wave data maps enables improved noninvasive localization of left atrial arrhythmias prior to radiofrequency catheter ablation. Noninvasive localization of left atrial arrhythmias is important since it can target and minimize invasive

10   catheter mapping to a small confined segment of the left atrium prior to ablation therapy delivery. Consequently, shorter and more efficient mapping and ablation procedures will result in less fluoroscopic exposure of the patient and physician as well as the patient will undergo less trauma and benefit from reduction in the procedure-related risk for clot formation and stroke. The database of the present invention can also be applied to

15   noninvasively screen patients and localize arrhythmias before admitting a patient to the electrophysiology laboratory to undergo ablation therapy. This noninvasive screening and arrhythmia localization can easily be performed in an outpatient clinic or physician's office and enables improved decision making regarding the optimal choice of therapy, e.g. anti-arrhythmic drugs, permanent pacing, or ablation treatment, or combinations of these treatment

20   modalities. Additionally, the database of the present invention also enables noninvasive follow-up of a patient to assess arrhythmia recurrences due to failure or disease progression after therapy delivery has taken place.

The embodiments of this invention relate to developing a database of mean multi-lead body

25   surface P wave data map patterns that can be used to classify and localize left atrial arrhythmias. Examples of currently known left atrial arrhythmias are atrial tachycardia, focal

11

atrial fibrillation, and orthodromic AV reentrant tachycardia involving an accessory pathway. The present invention may also be applied to other types of left atrial arrhythmias.

5   The use of body surface mapping allows ECG data presentation in a unique spatial format that contains a display of the P wave distribution on the entire torso surface. This electrocardiographic display format provides a better way to identify the focal source or reentrant circuit of atrial tachycardia, the focal source of atrial fibrillation, as well as the atrial insertion site of an accessory pathway with orthodromic AV reentrant tachycardia.

10   The method of the present invention is shown in the simplified flow diagram of **FIG. 1**. The electrical signal from a heart cycle **2** is a spontaneously occurring or induced left atrial arrhythmia or it can be obtained using left atrial pacing. One or more heart cycles **2** can be obtained in two or more subjects. The heart signal is received **4** as unipolar or bipolar ECG signals simultaneously obtained from an array of multiple electrodes on predetermined torso

15   sites. During signal processing **6**, leads with inferior signal quality are rejected and baseline adjustment is performed by linear interpolation. A series of potential maps of the P wave cycle is computed at 2-ms intervals (other intervals can also be used). In a potential map, the signal sensed at a time instant by sensors placed on a patient's torso is plotted on a representation of the torso, e.g. as a contour map or color map. P wave onset and offset are

20   determined, for instance, at the time instant when a peak reference voltage, e.g., 30 μV is reached and when the peak voltage drops below the reference voltage, respectively. Other criteria as well as an automated detection of P wave onset and offset can also be used. Subsequently, a body surface ECG P wave integral map is computed **8** over this selected time interval. In an integral map, the signal sensed by sensors is integrated over a selected time

25   interval and the integral is plotted on a representation of the torso, e.g. as a contour map or color map. Qualitative data classification **9** is carried out by grouping maps based on pattern

12

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similarity. Other methods of data classification based on, e.g. pattern recognition algorithms, neural networks, statistical routines or anatomical location of the left atrial ectopic origin, can also be used. Mathematical analysis using correlation coefficients is then performed to verify the qualitative data classification procedure. Furthermore, mean maps are computed **10** of the

5 classified maps. The mean maps (also called mean P wave maps) obtained during left atrial pacing or spontaneous or induced left atrial arrhythmias are stored in a database **12**. This unique database will then contain mean body surface P wave data maps for comparison to patient's body surface ECG P wave data maps to improve classification and localization of left atrial arrhythmias. The maps in the database provide a useful reference for localizing P

10 wave data from a patient with left atrial arrhythmias such as atrial tachycardia, focal atrial fibrillation, or orthodromic AV reentrant tachycardia using an accessory pathway. By comparing a patient's arrhythmia data to the maps in the database, a physician can provide a better diagnosis and make better decisions for a treatment regimen for an individual patient.

15 Referring to **FIG. 2**, there is shown by means of a more detailed general flow diagram the overall sequence of steps to develop a database of body surface ECG P wave data maps for classification and localization of left atrial arrhythmias. One or more heart cycle signals **20** are acquired in two or more subjects. The electrical heart cycle signal **20** is obtained during left atrial pacing or spontaneously occurring left atrial arrhythmias. Left atrial pacing is

20 performed using an electric stimulus probe such as a catheter using a transseptal or a retrograde aortic procedure. Alternative approaches or techniques other than a catheter are also feasible. Spontaneous left atrial arrhythmias can for example be atrial premature beats, atrial tachycardia, the initiating beat of focal atrial fibrillation, and the retrograde atrial activation during orthodromic AV reentrant tachycardia involving an accessory pathway.

25 Left atrial arrhythmias can also be induced by programmed stimulation, pharmacologic challenge, or other means.

13

In a particular embodiment, left atrial pacing is conducted at 79 pacing sites (higher and lower numbers can also be used) under biplane fluoroscopic guidance in the 45 degree right and 45 degree left anterior oblique projections. Other fluoroscopic projections or other imaging

5   techniques may also be used. A pacing protocol is aimed at accumulating pacing sites in key anatomical structures (i.e. pulmonary veins, around the circumference of the mitral annulus through the coronary sinus or directly from within the left atrium, the left atrial appendage, and the septum) as well as at obtaining additional coverage of the remainder of the left atrium. All pacing positions on the biplane fluoroscopic images are visually translated into positions

10   on an anatomical diagram of the left atrium while the pacing protocol is in progress or immediately after its completion.

The heart cycle signal **20** is processed by a P wave classification routine **21**. At step **22**, the heart signal is received as unipolar or bipolar ECG signals simultaneously obtained from an

15   electrode array on predetermined torso sites. Referring to **FIG. 5A**, the techniques of the present invention will generally make use of an array **100** of sensors **112** distributed across anterior and posterior skin surfaces of torso **T** on patient **P**. Array **100** provides multi-lead ECG data at a plurality of sensing locations distributed across the torso **T**, typically at over 20 sensing locations, more preferably at over 40 sensing locations, and ideally at 62 or more

20   sensing locations.

Sensors **112** generally comprise unipolar or bipolar electrodes coupled to the patient's skin, or to an alternative accessible body surface (for example via a transesophageal approach) suitable for measuring electrical body surface potential. Suitable electrode structures may

25   include those described in U.S. Patent Nos. 5,311,873 and 5,634,469, which are incorporated

herein by reference. Alternative sensor array structures and associated data acquisition and manipulation components may also be used.

5   ECG data is preferably acquired simultaneously from each of sensors **112** of array **100** at a sampling rate of over about 500 Hz, ideally at a sampling rate of about 1,000 Hz or more. In some embodiments, sequential sampling of sensors **112** from array **100** may alternatively be used, and higher or lower sampling rates also are feasible. When a lower sampling rate is used, the data may be upsampled using multirate filter banks.

10   Referring to **FIG. 2,** at step **24,** if the P wave is obscured, e.g., due to the P wave activity coinciding with ventricular recovery of the preceding cardiac cycle, the QRST subtraction **26** routine can be invoked to separate the signals. It may be possible in some circumstances to artificially separate the P wave from the QRST interval, i.e., by the use of pharmacological compounds that temporarily block AV conduction or by electrical pacing of the ventricle. 15   Alternatively, other signal separation methods and systems may also be used.

Referring to **FIG. 3**, the QRST subtraction routine **26** uses an adaptive QRST template constructed from averaged QRST complexes obtained from body surface ECG measurements to enable isolation of the otherwise obscured P wave activity.

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The method of **26** generally includes recording of unipolar or bipolar ECG data from the array of torso sites in steps **50** and **54**. The signal **50** is obtained during left atrial pacing or during a spontaneous or induced left atrial arrhythmia that contains electrical heart signals in which atrial activity is obscured by ventricular activity. This recorded signal **50** will also include 25   both the P wave and a superimposed QRST signal portion **52** and is further referred to as the obscured P wave signal. The method **26** also receives at least two template signals **54** that

contain electrical heart signals obtained during normal sinus rhythm or atrial overdrive pacing for the construction **56** of a QRST template **57**. In the exemplary embodiment, about 100 cardiac cycles of 62-channel unipolar ECG data are recorded, although fewer cycles may be used if the spatial and temporal variations of the QRST complex are relatively low.

5   Typically, more than ten cycles will be used, often more than 50 cycles for construction **56** of the QRST template **57**.

An adaptation of the QT interval of the QRST template can take place to correct for differences in heart rate with the obscured P wave signal. One or more fiducial points and windows are identified and annotated **58** for both the QRST template to create a so called annotated QRST template as well as for the obscured P wave signal, to create a so called annotated obscured P wave signal. Alignment **60** of the one or more fiducial points and windows annotated in the annotated QRST template and the annotated obscured P wave signal then takes place. After the alignment **60** of the annotated QRST template and annotated obscured P wave signal, the annotated QRST template is resampled and modulated **62** to further compensate for remaining discrepancies in duration and/or voltage. This creates a resampled and modulated QRST template. The atrial activity contained in the obscured P wave signal is isolated by subtracting **64** the resampled and modulated QRST template from the obscured P wave and thereby generating an isolated P wave **66**. It is important to realize

20   that the QRST template is adaptive to optimize the subtraction by first aligning the QRST template and then resampling and modulating the QRST template. The reason is to account for a discrepancy in heart rate and voltage amplitude of the QRST template with the TU complex of the obscured P wave signal. The method **26** includes a variety of techniques that can be used to modulate and resample the QRST template. Generally, this approach of

25   modulation and resampling allows for the surface ECG measurements to retain their intricate spatial and temporal detail within the P wave morphology. The method **26** is capable of

unmasking and preserving subtle electrical heart signal details of the relatively low-voltage P

wave despite the obscuring superimposed relatively high-voltage QRST complex.

Further details of QRST subtraction method **26** are described in, and are incorporated herein

5   by reference, U.S. Patent Applications Serial Nos. 09/809,719 and 09/808,728, both filed

March 14, 2001.

Referring to **FIG. 2**, all lead tracings are screened at step **28** in order to reject poor quality

signals or signals from lead sites that are dislodged or obscured by defibrillation patches on

10   the front and back of the subject's chest. The details of the signal-processing step **30** are

depicted in the flow diagram of **FIG. 4.** All lead tracings are visually or automatically

screened for signal quality **70**. Absent signals **72** are detected and deleted **74**, and substitute

values **76** are interpolated based on adjoining lead recordings. Poor quality signals **77** are

detected and rejected **78**, and substitute values **80** are interpolated based on adjoining lead

15   recordings. Interelectrode offset differences **82** are corrected **84** and linear baseline drift **86** is

corrected **88**. Both the offset and drift may be corrected **84, 88** by using linear interpolation

after selecting one or more isoelectric time instants or intervals. Digital filtering to remove

line frequency interference **90** is performed when necessary with a filter **92** such as a 60-Hz

notch filter or other type of filter. Other means of filtering can also be used. The end result

20   of the signal processing **30** is a good quality signal **94**.

Referring to **FIG. 2**, by way of example, P wave integral maps are computed **32** as follows.

Electrocardiographic data is analyzed by determining the onset and offset of the P wave.

Subsequently, an integral map is computed over this selected time interval. Referring to **FIG.**

25   **5C**, graph **114** includes an ECG signal tracing **116** representing the variation in voltage over

time. Signal tracing **116** may be used to evaluate heart cycle signals. In general, one or more

reference heart cycles will be selected for manipulation and comparison. ECG tracing **116** can be used to determine an onset (starting time) **118** and offset (ending time) **120** of a time interval **122** of the heart signal cycle that is of interest for evaluating one or more regions of the heart. For instance, P wave onset and offset can be determined at the time instant when a

5   peak reference voltage, e.g., 30 μV is reached and when the peak voltage drops below the reference voltage, respectively. Alternative criteria for determining P wave onset and offset might also be used, and automated detection of time interval **122** is also feasible. Instead of a time interval, single or multiple time instants in the P wave cycle may also be selected.

10   **FIG. 5A** shows an exemplary map of sensor locations **112** on the front and back of a subject's torso. **FIG. 5B** shows an exemplary plot of a data matrix generated by mapping the integral values with positions corresponding to the location of the sensors **112** across a torso **T** of a patient **P** in **FIG. 5A**. **FIG. 5C** shows the calculation of an integral value from a plot **114** of heart cycle signal **116**. In the exemplary embodiment of **FIG. 5C**, a P wave integral

15   numerical value may be calculated based on heart cycle signals **116** within selected time interval **122** having an onset **118** and an offset **120** for a particular sensor location **N10**. This calculated P wave integral value reflects the time/amplitude area of ECG signal at the sensor location within the selected time interval. Similar integral values are calculated for each sensor location, and the sensor values are mapped within data matrix **124** continuously from a

20   portion of the data matrix associated with a front **F** of torso **T**, across a side of the patient **P**, and to a back **B** portion of torso **T**. As shown in **FIG. 5B**, the data matrix will often be presented graphically by calculating and plotting lines of constant integral values **128** based on the individual discrete integral values and their associated positions within the data matrix. In some embodiments, this information can be summarized by presenting a single line **130** of

25   zero integral value between a region of positive integral values **132** and a region of negative integral values **134**. Alternatively, 3-D or chest anatomy-based representations of the data

matrix and/or color plots may be used to represent the data matrix wherein different colors represent different integral values or ranges of integral values. Of course, contour maps or color plots of potential values that represent P wave data may also be plotted as set forth above.

5   Referring again to **FIG. 2**, the P wave data maps are classified visually at step **33** according to a correspondence in the spatial location and mutual orientation of its map extremes and zero line configuration. This will result in one or more groups of P wave data maps with nearly identical P wave morphology. Alternative methods to classify and group the P wave data maps, e.g. pattern recognition algorithms, neural networks, statistical analysis or an

10   anatomical subdivision of the location of the left atrial ectopic origin, may also be used. At step **34**, quantitative data verification is carried out by subjecting the groups of P wave data maps to a mathematical analysis using correlation coefficients in order to compare the uniformity of the P wave pattern within each group and the variability of the P wave pattern between groups. Other methods of quantitative data evaluation, statistical or the like, may

15   also be used.

Mean maps are then computed at step **36** to form for instance mean P wave integral maps from a group of nearly identical P wave integral maps obtained in different patients. **FIG. 6**, depicts a group of nearly identical P wave body surface integral maps obtained during pacing

20   at the left upper (site A **610** , B **620,** D **640,** E **650** and F **660**) and left lower pulmonary vein (site C **630**). The displayed map patterns are all spatially compatible with regard to the location and orientation of the extremes and zero line contour.

Referring again to **FIG. 2**, the mean P wave data maps are stored in reference database **38**.

25   Database **38** contains mean P wave maps of a variety of ectopic origins in the left atrium. The ectopic origin of each mean map is determined for left atrial pacing as well as for

spontaneously occurring or induced left atrial arrhythmias. In case of left atrial pacing, biplane fluoroscopy or other imaging modality is used, such as e.g. ultrasound, to determine the anatomical location of the pacing that was performed with a probe or catheter. In case of spontaneously occurring left atrial arrhythmias, similar imaging techniques can be used, while

5 multipolar catheter electrogram recordings or alternative methods are used to determine the origin of the arrhythmias.

P wave body surface ECG integral maps of a given patient's left atrial arrhythmia **42** can subsequently be compared at step **44** to the reference database **38** to classify and localize the

10 origin of that patient's left atrial arrhythmia. Consequently, a unique database is available for improved classification and localization of left atrial arrhythmias. The resolution of the database can always be updated and improved by adding new and/or more detailed information related to the P wave data and the underlying ectopic origin sites.

15 Referring to **FIG. 7,** an exemplary database of 17 different mean P wave integral map patterns is shown generated by left atrial pacing. Higher or lower number for the groups with nearly identical P wave morphology can also be used. A higher number of groups improves the resolution of the database and thereby of the classification and localization of the left atrial arrhythmias. The encircled numbers **710 (710A, 710B,** and **710C)** relate maps to a

20 specific endocardial segment of pacing origin shown in the anatomical diagrams **720 (720A, 720B** and **720C).** Endocardial segments of pacing can also be delineated as single points, clusters of points, or the like. Other anatomical or schematic diagrams of the left atrium can also be used. Representation of the endocardial segments of pacing may also include biplane fluoroscopic views. The mean P wave integral map display features extreme positions and

25 zero line contour without positive and negative contour lines. Different forms of map format (e.g. 3-D or chest anatomy-based format) or map display (e.g. use of various color schemes)

can also be used. The three dimensional diagrams offer a postero-anterior (PA, **720A** in **FIG. 7A**), an anteroposterior (AP, **720B** in **FIG. 7B**), and a left posterior oblique view (LPO, **720C** in **FIG. 7C**) of the left atrium. Major anatomical landmarks are highlighted: the left (LPA) and right (RPA) pulmonary artery; the superior (SVC) and inferior (IVC) vena cava; the left

5   atrial appendage (LAA); right atrium (RA); coronary sinus (CS); the left ventricle (LV); the left upper (LUPV), left lower (LLPV), right upper (RUPV), and right lower (RLPV) pulmonary vein; Bachmann's bundle (BB); mitral annalus (MA); anterior mitral valve leaflet (AMV); and the fossa ovalis (FO).

10   Referring to **FIG. 8**, the design of an apparatus **140** for classifying and localizing left atrial arrhythmias is described. The apparatus **140** obtains data for development of a database by recording unipolar or bipolar ECG tracings from a plurality of predetermined torso sites on a subject **150**. In a preferred embodiment, the tracings are obtained from an array of 62 unipolar electrodes during spontaneously occurring or induced left atrial arrhythmia or left atrial

15   pacing. Alternatively, a smaller or larger number of electrodes or a different distribution of electrodes on the torso can also be used.

Electrocardiographic data from the electrodes are received by a signal processor **152**. The electrocardiographic data may be acquired simultaneously by the signal processor **152** at a

20   1000 Hz sampling rate using a multi-lead ECG recording system. Alternatively, the signal processor can perform sequential sampling. Other data rates may also be used. The data can be upsampled using multirate filter banks when a lower sampling rate is used. The signal processor **152** may delete absent signals due to electrode obscurement by defibrillator patches or lead dislodgment. The signal processor **152** may automatically identify and reject poor

25   quality signals. Alternatively, poor quality signals may be visually identified and rejected. These rejected signals may be substituted by interpolating adjacent lead recordings. The

signal processor may also correct for interelectrode offset differences and linear baseline drift,

e.g., using linear interpolation after selecting one or more isoelectric time instants or intervals

(other techniques for baseline adjustment can also be used). The signal processor **152** may

incorporate digital filtering to remove line frequency interference when necessary, e.g., with a

5   60-Hz notch filter (other types of filter or means of filtering may also be used).

A computing means **154** coupled to the signal processor **152** computes one or more maps **153**,

e.g., potential maps, of the P wave, e.g., at 2-ms intervals (other intervals can also be used).

The potential maps are visually evaluated to determine P wave onset and offset as the point in

10   time when one of the extreme values supersedes and returns within a 30 μV reference voltage

window around the zero line. Alternatively, other criteria for P wave onset and offset can

also be used as well as the onset and offset can be automatically detected. In a particular

embodiment, an integral map **153** of the selected time interval in the P wave cycle is

computed. As an alternative, the computing means **154** may compute P wave potential maps

15   at single or multiple selected time instants. The computing means **154** may include software

or hardware or some combination of both. Furthermore, the computing means may be

incorporated into signal processor **152**.

A validating means **156** then validates the patterns in the maps **153**. The validating means

20   typically includes circuitry or software for waveform analysis or filtering to determine if a

given map pattern makes sense. For example, the validating means may reject any map for

which the integral or potential values lie outside of a predetermined range. Alternatively, the

validating means **156** may display the map for visual inspection by an expert.

25   A classifying means **166** classifies one or more groups of P wave data maps with nearly

identical P wave morphology. Alternative methods to classify and group the P wave data

maps, e.g. pattern recognition algorithms, neural networks, statistical analysis or an anatomical subdivision of the location of the left atrial ectopic origin, may also be used. Once the maps **153** have been classified in groups based on pattern resemblance, a verifying means **165** will mathematically evaluate group selection using correlation coefficients to compare

5 intragroup pattern uniformity and intergroup pattern variability. The verifying means **165** may also perform statistical analysis on the map patterns in the groups **153**, e.g. to determine if the map patterns lie within a statistical margin for error. Subsequently, an averaging means **167** averages the classified maps that lie in the same classification. The mean maps are then stored in the reference database **170**. Classified map patterns from a plurality of subjects **150**

10 build up the database **170**. Once the database contains a sufficient number of mean map patterns, the apparatus **140** may be used to classify and localize **172** a left atrial arrhythmia in a patient **151** by comparing **171** P wave map patterns **153B** from the patient with the mean P wave map patterns in the database **170**. The P wave maps **153B** (e.g. potential or integral maps) of patient **151** are obtained in a similar way as for the generation of the database **170** as

15 shown in **FIG. 8**. This means that electrocardiographic data from the patient **151** is received by a signal processor **152B**, and a computing means **154B** to compute one or more maps **153B**.

Referring to **FIG. 9**, an embodiment of the invention can be implemented as computer

20 software in the form of computer readable code executed on a general purpose computer such as computer **201**, or in the form of bytecode class files running on such a computer. A keyboard **210** and a mouse **211** are coupled to a bi-directional system bus **218**. The keyboard and mouse are for introducing user input to the computer system and communicating that user input to processor **213**. Other suitable input devices may be used in addition to, or in place of,

25 the mouse **211** and keyboard **210**. I/O (input/output) unit **219** coupled to bi-directional system bus **218** represents such I/O elements as a printer, A/V (audio/video), I/O, etc.

Computer **201** includes a video memory **214**, main memory **215** and mass storage **212** (database storage), all coupled to bi-directional system bus **218** along with keyboard **210**, mouse **211** and processor **213**. The mass storage **212** may include both fixed and removable

5   media, such as magnetic, optical or magnetic optical storage systems or any other available mass storage technology. Bus **218** may contain, for example, thirty-two address lines for addressing video memory **214** or main memory **215**. The system bus **218** also includes, for example, a 32-bit data bus for transferring data between and among the components, such as processor **213**, main memory **215**, video memory **214** and mass storage **212**. Alternatively,

10   multiplex data/address lines may be used instead of separate data and address lines.

In an embodiment of the invention, any suitable microprocessor or microcomputer may be utilized as processor **213**. Main memory **215** may be a random access memory (RAM), dynamic random access memory (DRAM) or an equivalent. The main memory **215** typically

15   contains a program **230** having instructions executable by the processor **213**. In a preferred embodiment, the program **230** contains processor executable instructions that implement the steps of the method **1** of **FIG. 1** or method **21** of **FIG. 2**. Alternatively, the program **230** may be stored wholly or partly in the mass storage **212**. The mass storage **212** may contain database **232** of mean P wave maps for use with the program **230**. The database may have

20   features in common with the database **38** and **170** described above in relation to **FIG. 2** and **FIG. 8**, respectively.

Video memory **214** may be a dual-ported video random access memory. One port of the video memory **214** is coupled to video amplifier **216**. The video amplifier **216** is used to

25   drive the display **217** (i.e. CRT, LCD). The video amplifier and the monitor may be implemented by any suitable apparatus.

Computer **201** may also include a communication interface **220** coupled to bus **218**. Communication interface **220** provides a two-way data communication coupling via a network link **221** to a local network **222**. For example, if communication interface **220** is an

5   integrated services digital network (ISDN) card or a modem, communication interface **220** provides a data communication connection to the corresponding type of telephone line, which comprises part of network link **221**. If communication interface **220** is a local area network (LAN) card, communication interface **220** provides a data communication connection via network link **221** to a compatible LAN. Wireless links are also possible. In any such

10   implementation, communication interface **220** sends and receives electrical, electromagnetic or optical signals that carry digital data streams representing various types of information.

Network link **221** typically provides data communication through one or more networks to other data devices. For example, network link **221** may provide a connection through local

15   network **222** to a local server computer or host **223** or to data equipment operated by an Internet Service Provider (ISP) **224**. ISP **224** in turn provides data communication services through the world wide packet data communication network now commonly referred to as the "Internet" **225**. Local network **222** and Internet **225** both use electrical, electromagnetic or optical signals that carry digital data streams. The signals through the various networks and

20   the signals on network link **221** and through communication interface **220**, which carry the digital data to and from computer **201**, are exemplary forms of carrier waves transporting the information.

Computer **201** can send messages and receive data, including program code, through the

25   network(s), network link **221**, and communication interface **220**. In the Internet example, remote server computer **226** might transmit a requested code for an application program or

specific electrocardiography database through Internet **225**, ISP **224**, local network **222** and communication interface **220**. Consequently, they provide an important link for rapid medical information exchange such as telemedicine.

5   The received code may be executed by processor **213** as it is received, and/or stored in mass storage **212**, or other non-volatile storage for later execution. In this manner, computer **201** may obtain application code in the form of a carrier wave.

Application code (i.e. database, procedures, etc.) may be embodied in any form of computer program product. A computer program product comprises a medium configured to store or transport computer readable code, or in which computer readable code may be embedded. Some examples of computer program products are CD-ROM disks, ROM cards, floppy disks, magnetic tapes, computer hard drives, servers on a network, and carrier waves.

15   The computer systems described are for purposes of example only. An embodiment of the invention may be implemented in any type of computer system or programming or processing environment.

The ability to rapidly acquire, store, analyze and share medical information is necessary considering the rapid rate of change in medical technology. This computer **201** embodiment provides a database system capable of acquiring, analyzing, displaying and storing patient data in real time locally. In addition, communicating with other medical research centers allows sharing of medical information which can add new techniques and enlarge the subject database by the addition of new data elements from other centers.

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It will be clear to one skilled in the art that the above embodiment may be altered in many ways without departing from the scope of the invention. Accordingly, the scope of the invention should be determined by the following claims and their legal equivalents.